Comment in response to CrossTalk debate:

Skeletal muscle oxidative capacity is/is not altered in patients with cystic fibrosis

Multimodal exercise evaluation is needed to truly determine the functional consequences of altered skeletal muscle oxidative capacity in cystic fibrosis

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As the evidence supporting metabolic deficiencies within skeletal muscle in cystic fibrosis (CF) grows, further consideration should be given to evaluating the potential clinical implications of these abnormalities. Specifically, it is important to determine how alterations at the cellular level may impact peripheral muscle function (e.g. strength, endurance and fatigability, e.g. Gruet *et al.* 2017). Studies exploring oxidative metabolism during upright cycling and cycling during ^{31}P-magnetic resonance spectroscopy have provided crucial insight how central and peripheral factors may modulate oxidative metabolism in CF (Saynor *et al.* 2016; Werkman *et al.* 2016). However, such exercise testing does not permit us to fully infer the functional consequences of myocyte metabolic abnormalities to the locomotor muscles, since whole-body assessments of oxidative capacity may also reflect factors not specifically related to muscle (e.g. cardiac and/or pulmonary). Tasks that specifically localise a muscle group (e.g. quadriceps) with minimal cardiorespiratory constraint are thus also needed. Testing should ideally assess local muscle endurance and fatigability, by performing dynamic or isometric contractions at a relative intensity (percentage of maximal voluntary force), to control for differences in strength and/or muscle volume (often reduced in CF) (e.g. Gruet *et al*. 2016). However, as local exercise may not reflect day-to-day activities, we suggest a combined approach, assessing the relationship with whole-body exercise, is important. Using these complementary approaches will enable us to rule out or confirm the skeletal muscle metabolic abnormalities characterising CF and, importantly, their functional consequences. Multimodal assessments of aerobic fitness and skeletal muscle function, using reproducible tests (e.g. Bachasson *et al.* 2013; Saynor *et al.* 2013), represent an important next step in our understanding of how altered oxidative metabolism affects physical function in CF.

Competing interest

None declared

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